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10/574,489	07/25/2006	Yosuke Funakoshi	Q94183	9109

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EXAMINER	
CARTER, KENDRA D	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,489	FUNAKOSHI ET AL.	
	Examiner	Art Unit	
	KENDRA D. CARTER	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,24-27,29,30 and 32-35* is/are pending in the application.

4a) Of the above claim(s) *4, 17-21, 24-27, 30, and 32-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-16,29 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/3/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-21, 24-27, 29, 30 and 32-35, and the species election of cerebral infarction, in the reply filed on July 8, 2009 is acknowledged. The requirement is still deemed proper and is therefore made FINAL.

Claims 4, 17-21, 24-27, 30 and 32-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group and/or species, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1) Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cerebral infarction, does not reasonably provide enablement for preventing a neurodegenerative disease. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of preventing and/or treating a neurodegenerative disease, neuropathy or a disease whose treatment requires neural regeneration comprising administering an effective amount of (2R)-2-propyloctanoic acid. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method for preventing and/or treating a neurodegenerative disease, neuropathy or a disease whose treatment requires neural regeneration, which comprises parenterally administering to a mammal an effective amount of (2R)-2-propyloctanoic acid or a salt thereof."

(2) The breadth of the claims:

Claim 1 embraces and reads on preventing all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration. The specification does not enable the prevention of all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration.

(3) The state of the prior art:

The state of the art regarding preventing all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration is very low or do not exist. Weinreb (Can J Ophthalmol, 2007, vol. 42, no. 3, pp. 396-398) teaches that neuroprotection was initially investigated to treat disorders of the central nervous system (e.g., stroke, head trauma, amyotrophic lateral sclerosis, Parkinson's and Alzheimer's diseases), but only the minority of these investigations have led to approved therapies (see page 397, column 2, last paragraph to page 398, paragraph 1). There has not yet been proof of clinical efficacy for any neuroprotective agent in glaucoma (see page 398, clinical trials of glaucoma neuroprotection , paragraph 1).

(4) The predictability or unpredictability of the art:

The predictability of preventing all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration is relatively low. Therefore, to

one skilled in the art, prevention of all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high as demonstrated by Weinreb.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the prevention of all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that prevent all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read on the prevention of all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration. As discussed above the specification fails to provide any support for completely preventing all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at 1366 states that " a

patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for treating cerebral infarction, but not for preventing all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration.

2) Claims 1, 2 and 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cerebral infarction, does not reasonably provide enablement for treating all neurodegenerative disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of preventing and/or treating a neurodegenerative disease, neuropathy or a disease whose treatment requires neural regeneration comprising administering an effective amount of (2R)-2-propyloctanoic acid. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when

assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method for preventing and/or treating a neurodegenerative disease, neuropathy or a disease whose treatment requires neural regeneration, which comprises parenterally administering to a mammal an effective amount of (2R)-2-propyloctanoic acid or a salt thereof."

(2) The breadth of the claims:

Claims 1 and 2 embrace and read on treating all neurodegenerative disease. The specification does not enable the treatment of all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration.

(3) The state of the prior art:

The state of the art regarding effectively treating all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration is very low. Weinreb (Can J Ophthalmol, 2007, vol. 42, no. 3, pp. 396-398) teaches that

neuroprotection was initially investigated to treat disorders of the central nervous system (e.g., stroke, head trauma, amyotrophic lateral sclerosis, Parkinson's and Alzheimer's diseases), but only the minority of these investigations have led to approved therapies (see page 397, column 2, last paragraph to page 398, paragraph 1). There has not yet been proof of clinical efficacy for any neuroprotective agent in glaucoma (see page 398, clinical trials of glaucoma neuroprotection , paragraph 1).

(4) The predictability or unpredictability of the art:

The predictability of treating all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration is relatively low. Therefore, to one skilled in the art, treating all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration is unpredictable. In other words, just because there are potential therapeutic targets in treating all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration through the inhibition of S-100β , effective treatment has yet to be completely established. As Weinreb teaches that neuroprotection was initially investigated to treat disorders of the central nervous system (e.g., stroke, head trauma, amyotrophic lateral sclerosis, Parkinson's and Alzheimer's diseases), but only the minority of these investigations have led to approved therapies (see page 397, column 2, last paragraph to page 398, paragraph 1). Therefore, there is no guarantee that the compound will be clinically effective to treat all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration. Therefore, because there is a

"potential", treating all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration, it is unpredictable.

(5) The relative skill of those in the art:

The relative skill in the art is fairly high, with the typical practitioner having a medical degree and/or an advanced degree in the biochemical, chemistry or pharmaceutical-related arts, as evidenced by Weinreb.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to treating all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that treat all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02. Particularly, the specification teaches that (2R)-2-propyloctanoic acid treat cerebral infarction and inhibits the increase of S-100β (see examples).

(7) The quantity of experimentation necessary:

The instant claims read on treating all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration. As discussed above the

specification fails to provide any support for treating all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation.

Particularly, the skilled practitioner would have to test the claimed compound fore treatment efficacy for each condition. For example, to test for treatment of the disease, a particular compound inhibiting the increase of S100β, and a suitable animal model and dosage regimen (dose amount, frequency, route of administration) would also have to be selected. If efficacy of the drug did not result, the dosage regime would have to be varied, for example by changing the dosage amount or route of administration, until efficacy was achieved. If no animal model of a condition is available for testing, then toxicity trials would have to be conducted before such testing could be conducted in humans to determine appropriate toxicity levels. If efficacy in the treatment of the condition was shown with the particular compound, then another compound having S100β inhibitory activity would have to be selected and the process would have to be repeated, including determining the optimum dosage regimen and animal model and/or toxicity levels for evaluation. Once efficacy was established, the process would have to be repeated for each condition. Thus, the skilled artisan would have to undergo exhaustive studies to evaluate for effective treatment of each condition, or at least a subset, in order to be able to fully carry out the invention commensurate in

scope with the claims.

Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for treating cerebral infarction, but not for treating all neurodegenerative diseases, neuropathy or diseases whose treatment requires neural regeneration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-7, 9-16, 29 and 35 rejected under 35 U.S.C. 102(b) as being anticipated by Tateishi et al. (Journal of Cerebral Blood Flow & Metabolism, June 2002, vol. 22, no. 6, pp. 723-734).

Using the permanent middle cerebral artery occlusion (pMCAO) model in rats, Tateishi et al. show that there is a significant increase in the infarct volume between 24 and 168 hours after pMCAO, which closely resembles the time course of infarct expansion in human stroke (see page 723, column 2, paragraph 2). Tateishi et al. teach that (R)-(-)-2-propyloctanoic acid (ONO-2506) leads to mitigation of delayed infarct expansion and early improvement of neurologic deficits (i.e. treatment of cerebral infarction; see title; addresses claims 1, 2, 5, 29 and 35). ONO-2506 also significantly reduced the expression of S-100β (see abstract, lines 3-4 and 11-12; addresses claim 16). The rats were administered intravenously 10mg/kg daily, in which significantly reduced the infarct volume at 168 hours (i.e. continuous intravenous administration for 7 days; see page 725, column 1, determination of the optimal dose of ONO-2506 experiment 1 and page 727, column 1, the therapeutic time window of ONO-2506: experiment 4; addresses claims 6, 7, 9-15 and 35).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 8 is rejected under 35 U.S.C. 103(a) as being obvious over Tateishi et al. (Journal of Cerebral Blood Flow & Metabolism, June 2002, vol. 22, no. 6, pp. 723-734) as applied to claims 1-3, 5-7, 9-16, 29 and 35 above in view of Shirasaki et al. (US 5,837,706).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention “by another”; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR

1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The teachings of Tateishi et al. are as applied to claims 1-3, 5-7, 9-16, 29 and 35 above.

Tateishi et al. does not specifically teach that the continuous inravenous administration is from an infusion bag.

Shirasaki et al. teach that a drug that treats cerebrovascular disorders such as cerebral infarction is preferably administered by intravenous drip infusion (i.e. infusion bag administration; see column 4, lines 44-47 and column 5, lines 7-9).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine use an infusion bag administration in the method of Tateishi et al. because Shirasaki et al. teach that cerebrovascular disorders such as cerebral infarction is preferably treated through the intravenous drip infusion

administration route (i.e. infusion bag administration; see column 4, lines 44-47 and column 5, lines 7-9).

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kendra D Carter/
Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627